UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/351,862	07/12/1999	PHILIP E. THORPE	4001.002282	1339

23720 7590 06/03/2004

WILLIAMS, MORGAN & AMERSON, P.C.
10333 RICHMOND, SUITE 1100
HOUSTON, TX 77042

EXAMINER	
SHARAREH, SHAHNAM J	

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 06/03/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/351,862	THORPE ET AL.	
	Examiner	Art Unit	
	Shahnam Sharareh	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 November 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14 and 20-30, 34-48* is/are pending in the application.

4a) Of the above claim(s) *2,13,30 and 36-38* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,12,14,20-29,34,35 and 39-48* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 2/12/04, 2/18/04, 9/22/03, 2/9/04, 3/31/04
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on November 26, 2003 has been entered.

Status of the Claims

Amendment filed on April 28, 2003 has been entered. Claims 1-14, 20-30, 34-48 are pending.

Claims 2, 13, 30, 36-38 are withdrawn from further consideration, as being drawn to a nonelected species. Applicant timely traversed the restriction (election) requirement in Paper No. 14, filed on February 20, 2002. However, claims 1, 3-12, 14, 20-29, 34-35, 39-48 are under consideration at this time.

This application contains claim 2, 13, 30, 36-38 drawn to an invention nonelected with traverse in Paper No. 14. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP, 821.01.

Applicant's arguments that are found to be relevant are addressed below along with the respective applicable rejection.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3-12, 14, 20-29, 34-35, 39-42 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Specifically, the disclosure lacks sufficient written description for compositions and kits comprising any or all types of antibodies that bind to any aminophospholipid and even further comprise such targeting antibodies that binds to surface expressed or localized components such as ICAM-1, PAMA, TIE, pleiotropin etc as recited in claims 22-25.

Examiner points out that the first paragraph of 25 USC 112 requires that the "specification shall contain a written description of the invention." This requirement is separate and distinct from the enablement requirement. *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1560, 19 USPQ2d 1111, 1114 (Fed. Cir. 1991). Accordingly, "the essential goal of the description of the invention requirement is to clearly convey the information that an applicant has invented the subject matter which is claimed." *In re Barker*, 559 F.2d 588, 592n.4, 194 USPQ 470, 473 n.4 (CCPA 1977). The instant application fails to meet such requirements by clearly setting forth how applicant is in clear possession of all multiple possibilities of the claimed kits.

In the instant case, the possession of the instant claimed invention as a whole is assessed based on the combined features of the claimed kits. Pages 168-178 sets forth various types of conjugates ant constructs that Applicant is indeed in possession. Such compositions comprise antibodies directed to VCAM and conjugates thereof. However, there is no other indication as to the type of construct hereby encompassed by the claims.

It is noted that the instant examples are neither exhaustive, nor define the claimed methods. There is no working example directing one of ordinary skill in the art to kits comprising an anti-phospholipid conjugate or unconjugate, and a second antibody composition for example directed to tumor or surface localized P-selectin or TIE receptor. Thus, one skilled in the art cannot reasonably conclude that the applicants had possession of the claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000.

Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 1, 3-12, 14, 20-22, 39-43 are rejected under 35 U.S.C. 102(e) as being anticipated by Schroit US Patent 6,300,308.

Schroit teaches antibody-therapeutic conjugates within the scope of the instant limitations, because Schroit teaches anti-PS antibody compositions in a kit form that can be administered seperately and at least each antibody composition of Schroit contains an antibody directed to PS and a polypeptide such as BCG or diphtheria toxoid. Schroit also specifically teaches kits that contains one or more lipid-conjugate or antibody compositoins (see col 7, line 40-col 9, line 30; col 20, lines 30-col 21, line 5; col 27, lines 35-col29, line 2; cliam 1-22). Schroit specifically discloses therapeutic kits comprising one or more lipid-conjugate antigens or antibodies directed to phosphatidylserine receptors in separate containers (col 7, lines 40-67; col 8, lines 1-40; col 28, lines 1-67); subsequently, the kits of Schroit contain at least two anticancer agents. Moreover,

Schroit teaches combination of his antibodies with a secondary anti cancer agents such as BCG or diphtheria toxoid (col 8, lines 65-67). Finally, Schroit discloses the use of humanized antibodies or recombinant antibodies in preparing his compositions (col 4, lines 33-49; col 13, lines 25-55). Thus, Schroit anticipates instant claims.

Applicant's arguments with respect to this rejection have been fully considered but are not found persusive.

As the initial matter, Applicant may not improperly attempt to narrow the scope of the claim by reading limitations of the specification into a claim or implicitly adding limitations which have no express basis in the claim. see *In re Morris*, 44 USPQ2d 1023, 1027-28 (Fed.Cir. 1997). In the instant case, the scope of claims 39-43 do not include any recitation towards a second anticancer agent that is "other than the first anti-cancer agent." Thus, at least with respect to these claims, Applicant is arguing unclaimed limitations and such arguments are moot on its face.

Second, the scope of the instant claims 1, 3-12, 14, 20-29, 34-35 are directed to kits containing at least a first anti-cancer agent comprising a first aminophospholipid antibody or antigen-binding fragment thereof and at least a second anti-cancer "other than said first antibody" that binds to an aminophospholipid. Examiner throughout the prosecution has interpreted such claims not to be limited to two distinct antibodies directed to aminophospholipids. Rather, consistent with the teachings of the specification and the plain language of the claim, the claims are directed to kits containing at least one anti-cancer agent that binds to an aminophospholipid, and a second anticancer agent that performs the same function.

According to the specification, the scope of a second anticancer agent "other than" at least a first antibody, encompasses a simple second dose of the first anti-cancer agent. Clearly,two separate doses are not the same as their respective single doses. To substantiate such interpretation of the claims, Examiner draws Applicant's attention to the instant specification at pages 19, 32 and which sets forth the scope of the limitations "at least first anticancer agents with at least a first antibody....." and at least a second anti-cancer agent other than said at least a first antibody." At page 19, the specification describes the term anti-aminophospholipids to include conjugate, unconjugate and naked antibodies.

At page 32, the specification defines the first limitation described above to be inclusive of anti-aminophospholipids and administeration of one or more of such antibodies. The specification further goes on to say that the first at least anticancer agent may be considered to be at least a second anti-cancer agent. (see lines 1-32). At page 35, the kit is defined to comprise a combined effective amount of an anticancer agent and an antibody that binds to an aminophospholipid.

Therefore, reading the meaning of such limitations in view of the specification indicates that two separate doses of the first anticancer agent meets the limitations of the instant claims, because the second cancer agent can be the same as the first cancer agent. Further, the recitaiton of "other than" has been given its plain meaning as not being the first dose and is viewed to be within the instant definiation of a combined effective amount of an anti-cancer agent an an antibody.

Schroit at col 7, line 67- col 8, line 1, states "In such cases, one or more containers would contain each of the PS composition(s).." Therefore, Schroit's discloses kits that can contain containers with a second anti-aminophospholipid antibody conjugate. Further, Schroit claims an antibody-therapeutic construct (see col6, line 65-col 7, line 11). Moreover, Schroit's antibody can exist in "separate moieties to be conjugated by user of the kit" (see col 6, lines 50-51). Thus, Schroit meets the limitations of the instant claims.

Applicant also argues that diphtheria toxoid of Schroit does not qualify as a therapeutic construct. In response, Examiner states that the instant specification at page 140, lines 4-10 identifies diphtheria toxins as an anti-cellular agents for therapeutic purposes. Thsu, Schroit provides therapeutic activity within the scope of the instant claims. Accordingly, Schroit anticipates the limitations of the instant claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 3-12, 14, 19-29, 34-35, 39-48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schroit US Patent 6,300,308 in view of Gimbrone US Patent 5,632,991 and Umeda (IDS, 9/19/1999) and Bayer US Patent 4,925,922.

The teachings of Schroit are described above. Schroit fails to use an unconjugated antibody in combination with a second anticancer agent and/or explicitly use a second anticancer agent different than the first dose of his first anticancer agent

Gimbrone discloses targeting agents conjugated to an antibody directed to ELAM-1 (E-Selectin), (col 5, lines 18-38). Gimbrone teaches that such endothelial specific adhesion molecules are rapidly unregulated on the surface of cultured human vascular endothelial cells (col 27, lines 59-67). Gimbrone also discloses the use of his targeting agent-therapeutic agent conjugate, alone or in combination with other antibody or antibody fragment and/or a therapeutic agent (a second anti-cancer agent) (col 15, lines 46-55). Therapeutic agents of Gimbrone produce apoptosis as they encompass

various toxins, antioxidants and anti-tumor drugs (see col 12-14, claim 2). Finally Gimbrone teaches that E-Selectin or a leukocyte-binding fragment thereof can be coupled to a chemotherapeutic drug that binds to tumor cell expressing receptors for E-Selectin, to kill the tumor cell (col 13, lines 58-67). Gimbrone also disclose methods for detecting E-Selectin expression within the body of a patient comprising steps of detecting E-Selectin by labeling the E-Selectin antibody with a radioactive isotope that can be detected under a scintillation counter (col 18, lines 60-65). Gimbrone does not teach the combination therapy of his antibody-therapeutic agent conjugate with an anti-aminophospholipids antibody.

Umeda teaches methods of producing monoclonal antibodies directed to phosphatidylserine of plasma membrane, and that patients with malignancy have a higher titer of anti-PS antibodies (see abstract, page 2273; 2nd col, 2nd paragraph, 2276). Umeda's teachings are used to show the conventional practice of preparing monoclonal antibodies directed to phosphatidylserine of outer cell membrane. Umeda does not teach the use of his antibodies in kits for diagnostic or therapeutic purposes.

Bayers is merely used to show the state of art with respect to using monoclonal antibodies conjugated to toxins alone or in combination with an unconjugated monoclonal antibody and the expectation of success in improving the clinical efficacy of such process. (see abstract, col 6, lines 44-55; col 23-25; col 33-35; col 38, lines 4-32).

The teachings of Schroit, Gimbrone, Umeda and Bayer are in the same field of endeavor as they are all directed to the field of antibody immunology.

It is *prima facie* obvious to combine two compositions each of which is taught by prior art to be useful for same purpose in order to form third composition that is to be used for very same purpose; idea of combining them flows logically from their having been individually taught in prior art. In *re Kerkhoven*, 205 USPQ 1069(CCPA) 1980. Accordingly, it would have been obvious to one of ordinary skill in the art at the time of invention to combine the antiphospholipid antibodies of Schroit with conjugates of Gimbrone in the same or distinct compositions, because the idea of combining them flows logically from their having been individually taught in prior art.

Further, Schorit encourages the use of his compositions in combination with other therapeutic modalities. Therefore, it would have been obvious to one of ordinary skill in the art at the time of invention to further add additional therapeutic modalities as taught by Gimbrone to improve the clinical efficacy of Schroit's kits. Furthermore, Umeda and Bayer are provided as more evidence on record to substantiate the expectation of success when preparing monoclonal antibodies directed to aminophospholipids and further using the combination therapy of two cytotoxic agents to improve the optimum clinical effect.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shahnam Sharareh whose telephone number is 571-272-0630. The examiner can normally be reached on 8:30 am - 6:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, PhD can be reached on 571-272-0629. The

fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

RUSSELL TRAVERS
PRIMARY EXAMINER
GROUP 1200